CLAIMS

1. An antibody comprising a variant heavy chain hinge region incapable of inter-heavy chain disulfide linkage.

2. The antibody of claim 1, wherein said variant heavy chain hinge region lacks a cysteine residue capable of forming a disulfide linkage.

3. The antibody of claim 2, wherein said disulfide linkage is intermolecular.

4. The antibody of claim 3, wherein said intermolecular disulfide linkage is between cysteines of two immunoglobulin heavy chains.

5. The antibody of any of claims 1-4 wherein a hinge region cysteine residue that is normally capable of forming a disulfide linkage is deleted.

6. The antibody of any of claims 1-4 wherein a hinge region cysteine residue that is normally capable of forming a disulfide linkage is substituted with another amino acid.

7. The antibody of claim 6 wherein said cysteine residue is substituted with serine.

8. The antibody of any of claims 1-7 which is a full-length antibody.

9. The antibody of claim 8, wherein said full-length antibody comprises a heavy chain and a light chain.

10. The antibody of any of claims 1-9, wherein said antibody is humanized.

11. The antibody of any of claims 1-9, wherein said antibody is human.

12. The antibody of any of claims 1-7 and 10-11 which is an antibody fragment.

13. The antibody of claim 12 wherein said antibody fragment is an Fc fusion polypeptide.

14. The antibody of any of claims 1-12, wherein said antibody comprises a heavy chain constant domain and a light chain constant domain.

15. The antibody of claim 1 which is selected from the group consisting of IgG, IgA and IgD.

16. The antibody of claim 15 which is IgG.

17. The antibody of claim 16 which is IgG1.

18. The antibody of claim 17 which is IgG2.

19. The antibody of any of claims 1-18 which is a therapeutic antibody.

20. The antibody of any of claims 1-19 which is an agonist antibody.

21. The antibody of any of claims 1-19 which is an antagonistic antibody.

22. The antibody of any of claims 1-18 which is a diagnostic antibody.

23. The antibody of any of claims 1-22 which is a blocking antibody.

24. The antibody of any of claims 1-23 which is a neutralizing antibody.

25. The antibody of any of claims 1-24 which is capable of binding to a tumor antigen.

26. The antibody of claim 25 wherein the tumor antigen is not a cell surface molecule.

27. The antibody of claim 25 wherein said tumor antigen is not a cluster differentiation factor.

28. The antibody of any of claims 1-24 which is capable of binding to a cluster differentiation factor.

29. The antibody of any of claims 1-24 which is capable of binding to a cell survival regulatory factor.

30. The antibody of any of claims 1-24 which is capable of binding specifically to a cell proliferation regulatory factor.

31. The antibody of any of claims 1-24 which is capable of binding to a molecule associated with tissue development or differentiation.

32. The antibody of any of claims 1-24 which is capable of binding to a cell surface molecule.

33. The antibody of any of claims 1-24 which is capable of binding to a lymphokine.

34. The antibody of any of claims 1-24 which is capable of binding to a cytokine.

35. The antibody of any of claims 1-24 which is capable of binding to a molecule involved in cell cycle regulation.

36. The antibody of any of claims 1-24 which is capable of binding to a molecule involved in vasculogenesis.

37. The antibody of any of claims 1-24 which is capable of binding to a molecule associated with angiogenesis.

38. The antibody of any of claims 1-37 which is aglycosylated.

39. The antibody any of claims 1-38 which is produced in a prokaryotic cell.

40. An antibody lacking inter-heavy chain disulfide linkage.

41. The antibody of claim 40, wherein said inter-heavy chain disulfide linkage is between Fc regions.

42. An immunoconjugate comprising the antibody of any of claims 1-41 conjugated with a heterologous moiety.

43. The immunoconjugate of claim 42, wherein said heterologous moiety is a cytotoxic agent.

44. The immunoconjugate of claim 43, wherein said cytotoxic agent is selected from the group consisting of a radioactive isotope, a chemotherapeutic agent and a toxin.

45. The immunoconjugate of claim 44, wherein the toxin is selected from the group consisting of calichemicin, maytansine and trichothene.

46. The immunoconjugate of claim 42, wherein said heterologous moiety is a detectable marker.

47. The immunoconjugate of claim 46, wherein said detectable marker is selected from the group consisting of a radioactive isotope, a member of a ligand-receptor pair, a member of an enzyme-substrate pair and a member of a fluorescence resonance energy transfer pair.

48. A composition comprising the antibody of any of claims 1-47 and a carrier.

49. The composition of claim 48 wherein the carrier is pharmaceutically acceptable.

50. A composition comprising the immunoconjugate of any of claims 42-47 and a carrier.

51. The composition of claim 50, wherein the carrier is pharmaceutically acceptable.

52. An article of manufacture comprising a container and a composition contained therein, wherein the composition comprises the antibody of any of claims 1-41.

53. An article of manufacture comprising a container and a composition contained therein, wherein the composition comprises the immunoconjugate of any of claims 42-47.

54. The article of manufacture of claim 52 or 53, further comprising instruction for using said composition.

55. A polynucleotide encoding the antibody or immunoconjugate of any of claims 1-46.

56. A polynucleotide encoding a variant immunoglobulin heavy chain incapable of inter-heavy chain disulfide linkage.

57. The polynucleotide of claim 56 wherein said variant heavy chain comprises a variant hinge region lacking a cysteine residue capable of forming a disulfide linkage.

58. A recombinant vector for expressing the antibody or immunoconjugate of any of claims 1-47.

59. A host cell comprising the recombinant vector of claim 58.

60. The host cell of claim 59 which is a prokaryotic cell.

61. The host cell of claim 60 which is a gram-negative bacterial cell.

62 The host cell of claim 61 which is E. coli.

63. The host cell of claim 62, further comprising a polynucleotide encoding at least one prokaryotic polypeptide selected from the group consisting of DsbA, DsbC, DsbG and FkpA.

64. The host cell of claim 63, wherein the polynucleotide encodes both DsbA and DsbC.

65. The host cell of claim 62, wherein the E. coli is of a strain deficient in endogenous protease activities.

66. A method comprising expressing in a host cell an antibody of interest in which at least one inter-heavy chain disulfide linkage is eliminated, and recovering said antibody from the host cell.

67. The method of claim 66, wherein at least two inter-heavy chain disulfide linkages of the antibody of interest are eliminated.

68. The method of claim 66, wherein all inter-heavy chain disulfide linkages of the antibody of interest are eliminated.

69. The method of claim 66, wherein said antibody comprises a variant hinge region of an immunoglobulin heavy chain, wherein said variant hinge region lacks at least one of the cysteine residues normally capable of forming a disulfide linkage.

70. The method of claim 69, wherein said variant hinge region lacks at least two of the cysteine residues normally capable of forming a disulfide linkage.

71. The method of claim 69 & 70, wherein said variant hinge region lacks all of the cysteine residues normally capable of forming a disulfide linkage.

72. The method of claim 69, wherein a cysteine of the hinge region normally capable of forming a disulfide linkage is deleted or substituted with another amino acid.

73. The method of claim 72, wherein said cysteine residue is substituted with serine.

74. The method of any of claims 66-73, wherein said antibody is a full-length antibody.

75. The method of any of claims 66-74, wherein said antibody is humanized.

76. The method of any of claims 66-75, wherein said antibody is human.

77. The method of any of claims 66-73 and 75-76, wherein said antibody is an antibody fragment.

78. The method of claim 77, wherein said antibody fragment is an Fc fusion polypeptide.

79. The method of any of claims 66-77, wherein said antibody comprises a heavy chain constant domain and a light chain constant domain.

80. The method of any of claims 66-79, wherein said antibody is selected from the group consisting of IgG, IgA and IgD.

81. The method of any of claims 66-68, wherein said antibody is selected from the group consisting of IgG, IgA, IgE, IgM and IgD.

82. The method of claims 80 or 81, wherein the antibody is IgG.

83. The method of claim 82, where said antibody is IgG1 or IgG2.

84. The method of any of claims 66-83, wherein said antibody is selected from the group consisting of therapeutic, agonist, antagonistic, diagnostic, blocking and neutralizing antibody.

85. The method of any of claims 66-84, wherein heavy and light chains of said antibody are encoded by a single polynucleotide.

86. The method of any of claims 66-84, wherein heavy and light chains of said antibody are encoded by separate polynucleotides.

87. The method of any of claims 66 to 86, further comprising determining that the antibody that is recovered is biologically active.

88. The method of any of claims 66 to 87, wherein the amount of said antibody of interest produced is at least about 10% greater than the amount of a reference antibody expressed under similar conditions, wherein said reference antibody has a wild type ability to form disulfide linkages.

89. The method of claim 88, wherein said antibody of interest comprises a variant immunoglobulin heavy chain hinge region lacking at least one of the cysteine residues normally capable of forming a disulfide linkage, and wherein said reference antibody comprises an immunoglobulin heavy chain hinge region that is the wild type counterpart of the hinge region of the antibody of interest.

90. The method of claim 88, wherein the amount is at least about 25%.

91. The method of claim 90, wherein the amount is at least about 50%.

92. The method of claim 91, wherein the amount is at least about 75%.

93. The method of any of claims 66-92, wherein the antibody of interest and reference antibody have substantially similar antigen binding capabilities.

94. The method of any of claims 66-92, wherein the antibody of interest and reference antibody have substantially similar FcRn binding capabilities.

95. The method of any of claims 66-92, wherein the antibody of interest and reference antibody have substantially similar pharmacokinetic values.

96. The method of any of claims 66-95, wherein said host cell is prokaryotic.

97. The method of claim 96, wherein said host cell is a gram-negative bacterial cell.

98. The method of claim 97, wherein said host cell is E. coli.

99. The method of claim 96, further comprising expressing in the host cell a polynucleotide encoding at least one prokaryotic polypeptide selected from the group consisting of DsbA, DsbC, DsbG and FkpA.

100. The method of claim 99, wherein the polynucleotide encodes both DsbA and DsbC.

101. The method of claim 98, wherein the E. coli is of a strain deficient in endogenous protease activities.

102. An aglycosylated antibody produced by the method of any of claims 66-101.

103. The method of any of claims 66-101, wherein said antibody is recovered from cell lysate.

104. The method of any of claims 66-101, wherein said antibody is recovered from culture medium or the periplasm.

105. A method comprising:

expressing in a prokaryotic host cell a variant immunoglobulin heavy chain,

said variant immunoglobulin heavy chain comprising a reduced ability to form a disulfide linkage such that amount of self aggregation of the variant immunoglobulin heavy chain is less than the amount of self aggregation of a reference immunoglobulin heavy chain when expressed under similar conditions,

wherein the reference immunoglobulin heavy chain has a wild type ability to form a disulfide linkage.

106. The method of claim 105, wherein said variant immunoglobulin heavy chain comprises a hinge region in which at least one cysteine is rendered incapable of forming a disulfide linkage and wherein the hinge region of the reference immunoglobulin heavy chain is the wild type counterpart of the hinge region of the variant heavy chain.

107. The method of claim 106, wherein at least two cysteines are rendered incapable of forming a disulfide linkage.

108. The method of claims 106, wherein all cysteines are rendered incapable of forming a disulfide linkage.

109. The method of any of claims 106 to 108, wherein said cysteine is normally capable of intermolecular disulfide linkage.

110. The method of any of claims 106-109, wherein the amount of aggregation of the variant heavy chain is at least about 10% less than the amount of self aggregation of the reference immunoglobulin heavy chain.

111. The method of claim 110, wherein the amount of aggregation of the variant heavy chain is at least about 25% less than the amount of self aggregation of the reference immunoglobulin heavy chain.

112. The method of claim 111, wherein the amount of aggregation of the variant heavy chain is at least about 50% less than the amount of self aggregation of the reference immunoglobulin heavy chain.

113. The amount of claim 112, wherein the amount of aggregation of the variant heavy chain is at least about 75% less than the amount of self aggregation of the reference immunoglobulin heavy chain.

114. The method of any of claims 105-113, wherein the host cell is prokaryotic.

115. A method of treating a disease in a subject comprising administering an effective amount of the antibody of any of claims 1-21 and 23-41 or the immunoconjugate of any of claims 42-45 to the subject, whereby said disease is treated.

116. A method of diagnosing a disease in a subject patient comprising contacting the antibody of any of claims 1-41 or the immunoconjugate of any of claims 46-47 with the subject or a tissue sample obtained from the subject, and determining amount of binding the antibody or immunoconjugate to an antigen in the subject or tissue sample, whereby a difference in amount of said binding compared to binding in a reference subject or tissue sample is indicative of presence or extent of the disease in the subject patient.

117. A method of delaying or preventing a disease in a subject comprising administering an effective amount of the antibody of any of claims 1-21 and 23-41 or the immunoconjugate of any of claims 42-45 to the subject, whereby said disease is delayed or prevented in the subject.

118. The method of any of claims 115-117 wherein the disease is a tumor.

119. The method of any of claims 115-117 wherein the disease is a cancer.

120. The method of any of claims 115-117 wherein the disease is an immune disorder.